

Iron Treatment Failure

According to the World Health Organization of the United Nations, iron deficiency anemia is the most common nutrition related disorder in the world today. It affects over 20% of the world population. Iron deficiency anemia occurs when hemoglobin levels drop below 12 g per 100 ml of blood. There are three stages in the development of iron deficiency anemia:

Stage One: Iron Depletion is characterized by a progressive reduction in the amount of storage iron in the liver. At this stage, transport iron and hemoglobin are normal, but serum ferritin is falling.

Stage Two: Iron Deficient Erythropoiesis is characterized by complete exhaustion of iron stores. This results in a progressive reduction of plasma iron supply to red blood cell production. Transferrin saturation decrease, while erythrocyte protoporphyrin increases (a precursor to heme, which accumulates when iron supply is not adequate for heme synthesis). Hemoglobin may decline slightly.

Stage Three: Iron Deficiency Anemia is caused by exhaustion of iron stores and declining levels of circulating iron. Frank microcytic, hypochromic anemia now develops. Hemoglobin declines, as well as hematocrit and all other red cell indices.

.....

The overall effectiveness of iron supplementation often hinges on the bioavailability of the iron form used, as well as the patient's compliance to the

iron regimen. The problem in predicting iron bioavailability lies in the factors that can inhibit the absorption of non-chelated forms of iron. The absorption and bioavailability of iron is complex. Iron absorption can take place throughout the intestine, but the duodenum and jejunum are the sites where the majority of iron is absorbed. Factors that inhibit absorption, particularly in the upper portion of the small intestine, would have the greatest effect on the bioavailability of iron.

Proper compliance can still result in treatment failure when non-chelated iron compounds are taken in conjunction with foods containing components that block the absorption of non-chelated iron¹. For example, polyphenols are secondary plant metabolites that inhibit non-chelated iron absorption^{2,3,4}. Tannins, found in tea, were the first polyphenols to be shown to have this effect. Later research has found that polyphenols in vegetables, such as sorghum and legumes, and in certain condiments, aggressively block non-chelated iron absorption⁵.

In addition to polyphenols, phytates found in cereals, nuts, and legumes have been seen to decrease non-chelated iron absorption^{6,7}. Plant proteins found in soybeans, nuts, and lupines, also contain other substances which can hinder non-chelated iron absorption as well.^{8,9,10,11,12}

Other interference to non-chelated iron absorption includes co-administration of

certain minerals, such as calcium, zinc, and copper, as well as many commonly used medications.

Due to the chemistry of iron and other transition metals, non-chelated iron has been shown to cause a great reduction in the bioavailability of many drugs by forming iron-drug complexes in the gut that are either not absorbed, or very poorly absorbed. In addition, non-chelated iron has been shown to catalyze reactions that destroy the activity of certain drugs. The functional groups on drugs that are known to bind strongly to iron include phenolic, catechol, carboxyl, amine, and sulphhydryl groups. Typically one iron ion will tie up to three drug molecules. It is important to note that only the ionized form of the iron from non-chelated or improperly chelated iron binds to, or inactivates, the drugs. Non-chelated iron can interfere with the absorption of drugs taken within two to three hours before or after the ingestion of the non-chelated iron products. Depending on the drugs and the amount of iron taken, the decrease in drug absorption due to iron has been seen to be anywhere from 50% to 88%.¹³

Enteric coated iron salts have been used to avoid the above problems, however, there have been reports that enteric coating of non-chelated iron products has resulted in poor hematologic response to the iron product. Researchers compared the bioavailability of iron from: iron solution, film coated iron tablets, and enteric

coated iron tablets. Blood samples were drawn hourly from 8 a.m. to 6 p.m. on the day before each study day to assess baseline serum iron concentrations on the study day. Spectrophotometry was used to determine serum iron. The bioavailability of iron from solution and from film coated tablets was equal. It was seen, however, that the iron from enteric coated tablets was absorbed at a rate that was only 30% of the other two dosage forms. The researchers concluded that, in view of these findings, enteric coated iron products should not be considered therapeutically interchangeable with film coated or oral solutions of iron.¹⁴

None of these factors are known to interfere with the chelated form of iron (Ferrochel®) produced by Albion Laboratories. Ferrochel's patented stability constant and electrical neutrality keep this chelated iron form from interacting with these substances in the gastrointestinal system, thus preventing their negative effects on Ferrochel's bioavailability.

Compliance was mentioned earlier as a second key to the treatment success of an iron supplementation regimen. Experience has clearly shown that unpleasant side effects are a leading cause of compliance failure. Iron supplements are notorious for causing abdominal discomfort and constipation. This does not occur with iron amino acid chelates produced by Albion Laboratories. Studies by Pineda¹⁵, Schruaffer and Steib¹⁶, Kirchoff¹⁷, and Schuette¹⁸, have all indicated that Albion's iron amino acid chelate is extremely well tolerated. The better the tolerance, the better the chance of patient compliance.

1. Baynes, R.D., Bothwell, T.H. "Iron Deficiency". *Ann Rev Nutr* 1990 Vol. 10 pp.133-148.
2. Bulier, L.G., Rieal, D.J., Lebryk, D.G., Blytt, H.J., 1984. "Interactions of Proteins with Sorghum, Tashin: Mechanism, and Specificity, and

- Significance." *J Am Oil Chem Soc*, 61: 916-20.
3. Dister, P.B., Lynch, S.R., Chariton, R.W., Torrance, J.D., Bothwell, T.H., et al., 1975. "The Effects of Tea on Iron Absorption," *Gut*. 16:193-200.
 4. Gillooly, M., Bothwell, T.H., Torrance, J.D., MacPhail, A.P., Derman, D.P., et al., 1983. "The Effects of Organic Acids, Phytates, and Polyphenols on Absorption of Iron from Vegetables." *Br J Nutr* 49:331-42.
 5. Rao, B.S., Prabhavathi, T., 1982. "Tannin Content of Foods Commonly Consumed in India and Its Influence on Ionizable Iron: *J Sci Food Agric*. 33:1-8.
 6. Halberg, L., Rossander, L., Skanberg, A.B., 1987. "Phytates and the Inhibitory Effect of Bran on Iron Absorption in Man," *Am J Clin Nutr*. 45:988-96.
 7. Halberg, L., Brune, M., Rossander, L., 1989. "Iron Absorption in Man in Man: Ascorbic Acid and Dose-Dependent Inhibition by Phylate," *Am J Clin Nutr*. 49:140-44.
 8. Cook, J.D., Morck, T.A., Lynch, S.R., 1981. "The Inhibitory Effects of Soy Products on Non-heme Iron Absorption in Man," *Am J Clin Nutr*. 34:2622-29.
 9. Derman, D.P., Ballot, D., Bothwell, T.H., Macfarlane, B.J., Baynes, R.D., et al. "Factors Influencing the Absorption of Iron from Soya-bean Products," *Br J Nutr*. 57:345-53.
 10. Macfarlane, B.J., Baynes, R.D., Bothwell, T.H., Schmidt, U., 1988. "The Effects of Lupines on Iron Absorption," *Eur J Clin Nutr*. 42:683-87.
 11. Macfarlane, B.J., Bezwoda, W.R., Bothwell, T.H., Baynes, R.D., Bothwell, J.E., et al, 1988. "Inhibitory Effects of Nuts on Iron Absorption," *Am J Clin Nutr*. 47:270-74.
 12. Macfarlane, B.J., Van der Riet, W.B., Bothwell, T.H., Baynes, R.D., Siegenberg, D., et al, 1990. "The Effect of Traditional Oriental Soy Products on Iron Absorption," *Am J Clin Nutr*. In Press.
 13. Campbell, N.R. and Hasinoff, B.B., *Br J Clin Pharmac*. (1991), 32:251-255.
 14. Walker, S.E., et al, *Can Med Assoc J*, Vol. 141, Sept 15, 1989, pp. 543-547.
 15. Pineda, O., et al, "The Effectiveness of Iron Amino Acid Chelate in the Treatment of Iron Deficiency Anemia in Adolescents." Publication pending. 1994 (AJCN).
 16. Schruaffer, H., Sten, W., "Experiences Treating Iron Deficiency Anemia with Iron Chelate Tablets," *Therapiewoche (Germany)* 1983. 33/15: 2121-23.
 17. Kirchoff, H.W., "Treatment of Iron Deficiency Anemia with Iron Chelate Tablets," *Therapiewoche (Germany)* 1983. 33/37: 4833-42.
 18. Schuette, S., "Tolerance of an Iron Chelate versus Ferrous Sulfate in Normal Women," In press.

Effectiveness of Ferrochel®

In a recent study, Dr. Oscar Pineda et al. found that 30 mg of elemental iron from Ferrochel was as effective in raising hemoglobin levels as 120 mg of elemental iron from ferrous sulfate. It was felt that this was due to the superior bioavailability of Ferrochel. (See Albion Research Notes®, Vol. 1, July 1992.)

With this in mind, Dr. Pineda et al., conducted a second study on infants suffering from iron deficiency anemia. The infants received 5 mg per kg of body weight of elemental iron, from Ferrochel or ferrous sulfate for 30 days. The changes in the infants' hemoglobin and ferritin can be seen in the chart below:

TREATMENT	CHANGES POST TREATMENT	
	Hemoglobin g/dl	Ferritin mcg/l
Ferrous Sulfate		
Ferrochel	+1.6 (+18%) +2.8 (+36%)	+26.6 (+61%) +74.4 (+139%)

Ferrochel was shown to increase hemoglobin levels of the anemic infant twice what was seen with ferrous sulfate. According to the data of Dr. Pineda et al., the iron from Ferrochel was being absorbed at an astounding rate of 75%, as compared to a 27.8% rate for ferrous sulfate.

Low Dose Iron Supplementation Does Not Cover the Need for Iron during Pregnancy

It has been well established that the need for iron substantially increases during pregnancy, especially during the third trimester. Studies have shown that the iron requirement in the third trimester is 8 to 10 mg per day over and above the US RDA. In theory, there is an iron requirement during pregnancy which is greater than the average iron stores found in fertile women. Studies have shown that pregnant women, without supplementation, deplete their iron stores and do not experience the increase in red cell mass seen in women receiving iron supplementation. Despite this, many feel that the benefits of iron supplementation during pregnancy have not been validated. Some, in fact, think

that routine iron supplementation during pregnancy could be harmful. Thus, many advocate low dose iron supplementation or screening in order to give selective iron prophylaxis.

In a study done to determine whether an 18 mg daily dose of iron (the US RDA) was sufficient to cover the iron need during normal pregnancy, nulliparae women with normal hemoglobin and intact iron stores at the 16th week of pregnancy were randomly selected to receive either 18 mg or 100 mg of non-chelated iron daily from the 16th week of pregnancy until delivery. Indicators of iron status were tested at the 16th, 30th, and 38th week of pregnancy. At week 30,

14% of the 100 mg group and 52% of the 18 mg group had depleted iron stores. The number of women with iron depletion was 5% (100 mg) and 72% (18 mg) at week 38. The study concluded that despite normal hemoglobin concentrations and intact iron stores in the 16th week of pregnancy, an iron supplementation of 18 mg of iron per day was not sufficient to cover the iron need in many pregnant women during the third trimester.

Thompson, J.K., et al., Octa Obstet Gynecol Scand. 1993, 72:93-98.

The Cost of Iron Supplementation from Different Sources

In a study conducted by Dr. Pineda, et al., on infants suffering from anemia, the investigators developed some very interesting data related to the cost of effective therapy for anemia. In the table below, data were presented showing the cost of the four weeks of iron therapy for the three commercially available iron products.

Dr. Pineda, et al., stated that the 74.4 mcg/l ferritin level reached with the Ferrochel product was indicative of a successful therapeutic effect, and one which would insure that the infants would have adequate stores of iron to stave off a repeat of anemia for some time. Based on the ferritin levels reached with the other two products, Iberol 500

and Fer-In-Sol, after the four weeks of therapy, the investigator extrapolated the length of time and cost that would be incurred to reach the level achieved by the Ferrochel product in 4 weeks. As can be seen in the table, the costs to achieve equal therapeutic success with the other two products were two to three times that seen with the Ferrochel product.

Cost of Anemia Treatment in Infants									
Product	Liquid Presentation ml (Total Fe, mg)	Fe mg/ml	Source of Iron	Unit Price	Price/mg Fe	Bio-availability	Total intake Std. Tx mg	Cost of Std. Tx	Cost of Tx to 74.4 mg/l Ferritin %
Intrafer (Unipharm)	150 (900)	6.00	Ferrochel® (Albion)	4.61	0.005	75.0	1059	\$5.48	\$5.48
Iberol-500 (Abbott)	120 (630)	5.25	FeSO ⁴	3.69	0.006	27.8	1059	\$6.22	\$17.40
Fer-in-Sol (Mead Johnson)	15 (375)	25.00	FeSO ⁴	1.87	0.005	27.8	1059	\$5.33	\$14.91

Bioavailability: Percent absorbed
Std. Tx=5 mg Fe/kg body weight/day for 30 days

REVIEW THE FACTS! Which Iron Form is Best?

In this edition of Albion Research Notes, a number of considerations regarding iron therapy have been brought to issue:

- Bioavailability
- Tolerance (lack of side effects)
- Effectiveness
- Cost of therapy
- Potential for interactions

Others exist as well, and will be dealt with in a later issue.

Albion's Ferrochel® has been shown in human clinical studies to have a bioavailability of approximately 75%, and was clearly superior to the other iron forms. In several human studies listed earlier, the researchers found Albion® iron amino acid chelate to be almost devoid of iron's usual gastric side effects (constipation, gastric upset, etc.).

Dr. Pineda, et al., found that Ferrochel produced superior improvement in red blood cell and iron storage indices, at much lower dosages. Data had been

provided to show Ferrochel raises hemoglobin and ferritin levels at a price far less than even the cheapest forms of non-chelated iron.

Last but not least, because of the patented manufacturing process, Ferrochel does not yield potentially negative dietary interactions as do other forms of iron, and does not exhibit the potential for drug interaction problems typical of other iron forms. All things considered, the choice is obvious. Ferrochel is the one.



Albion Human Nutrition

100 Maple Park Blvd., Suite 110
St. Clair Shores, Michigan 48081 USA
[P] 586•774•9055 | [TF] 800•222•0733
[F] 586•774•8838
[e] info@AlbionMinerals.com

© 2008 Albion Human Nutrition. All rights reserved.